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MEMORANDUM: RESPONSE TO ECOLOGICAL RISK ASSESSMENT FORUM REQUEST FOR INFORMATION ON THE BENEFITS OF PCB CONGENER-SPECIFIC ANALYSES

by

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF RESEARCH AND DEVELOPMENT
National Center for Environmental Assessment
Washington, DC 20460

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MEMORANDUM

SUBJECT: Response to the ERAF Request for Information on the Benefits of PCB Congener-Specific Analyses

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In August, 2001, the Ecological Risk Assessment Forum (ERAF) submitted a formal question to the Ecological Risk Assessment Support Center (ERASC) on the benefits of evaluating PCB congeners in environmental samples. This question was developed by ERAF members Bruce Duncan and Clarence Callahan. ERASC contacted NCEA's Exposure Analysis and Risk Characterization Group for assistance in responding to the request. The purpose of this memorandum is to formalize the response.

Central question being asked: *What information is provided by performing PCB congener analysis as compared with Aroclor or total PCB reporting of the results of environmental sampling?*

The production of PCBs ceased in the late 1970's. Monsanto produced commercial mixtures known as Aroclors that differed by the total amount of chlorine present as well as the PCB congener composition. In the environment, various biotic and abiotic processes shift the PCB congener composition from the original commercial products such that environmental samples no longer resemble PCB Aroclors. Hence using Aroclor technical standards to qualitatively determine PCB levels present in the environment may provide an inaccurate depiction of the current PCB congener mixtures present in environmental media and biota. This technical response is divided as follows:

I	A review of the historical production and use of PCBs
II	A brief review of the PCB congener composition of Aroclors
III	Alterations of PCB congener profiles as a result of environmental weathering
IV	Alterations of PCB congener profiles as a result of bioaccumulation and biomagnification in ecological food chains
V	Utility of PCB congener-specific analyses - an example
VI	Conclusions regarding PCB congener-specific analyses for environmental samples

I. Historical Production and Use of PCBs

As a prelude to the discussion of the benefits of congener-specific analysis, it is useful to briefly review the history of the domestic and global production and use of PCBs. PCBs were once perceived as highly valuable manmade chemicals. Their high boiling points and resistance to thermalytic breakdown made them useful in a broad array of industrial applications. Furthermore, since PCBs do not conduct electric current, they were useful for commercial purposes as insulating material and dielectric fluid. GThe global production of commercial PCB mixtures from 1929 to 1980 has been estimated to be greater than 1.1 million metric tons (Erickson, 1997). U.S. production has been estimated to be approximately 568,000 metric tons (U.S. EPA, 1976). Maximum U.S. production occurred in 1970 with a volume of 38,500 metric tons (IARC, 1978). In 1972, Monsanto Corporation, the major U.S. producer, voluntarily restricted the sale of PCBs to uses as dielectric fluids in "closed electrical systems." This restriction was prompted by growing evidence of PCBs' persistence in the environment, tendency to bioaccumulate in animal tissues and toxic effects. Annual production fell to 18,000 metric tons in 1974. Monsanto ceased PCB manufacture in mid-1977 and shipped the last inventory in October 1977 (Erickson, 19997). Regulations issued by EPA beginning in 1977, principally under the Toxic Substances Control Act (TSCA) (40 CFR 761), have strictly limited the production, import, use, and disposal of PCBs.

Monsanto Corporation marketed technical grade mixtures of PCBs primarily under the patented trade name Aroclor. The Aroclors are identified by a four-digit numbering code in which the last two digits indicate the approximate chlorine content of the formulation by weight percent. The exception to this coding scheme is Aroclor 1016, which contains only mono- through hexa-chlorinated congeners with an average chlorine content of 40 percent. The uses of Aroclors containing mixtures of PCB congeners can be classified into three categories (Erickson, 19997; U.S. EPA, 1976):

1. Completely closed electrical systems such as such as electrical capacitors and transformers. In these cases, PCB dielectric fluids are self-contained within the electrical apparatus in sealed steel vessels.

2. Semi-closed applications. In these cases, PCBs are used as lubricants in high temperature environments. Examples include hydraulic and heat transfer systems and vacuum pumps.

3. Open-ended applications. These uses are varied but refer to coatings, dyes, paints, inks, adhesives, pesticide extenders, plasticizers, synthetic rubber, carbonless copy paper,

cutting oils, lubricating oils, and casting waxes.

Estimates of PCB usage in the United States by usage category during the period 1930-1975 are presented in Table 1. Prior to voluntary restrictions by Monsanto Corporation in 1972 on sales for uses other than "closed electrical systems," approximately 13 percent of the PCBs were used in "semi-closed applications," and 26 percent were used in "open-end applications." Most of this usage of PCBs for "semi-closed" and "open-end" applications occurred between 1960 and 1972 (U.S. EPA, 1976). Table 2 shows the percentage of total aroclor production contributed by specific aroclors during the years 1957-1977. EPA has estimated that approximately 5 percent of the PCBs used in closed electrical systems were released into the open environment; 60 percent of the PCBs used in semi-closed applications were released; 25 percent of the PCBs used for plasticizers were released; and 90 percent of PCBs used for miscellaneous industrial uses had escaped into the environment (U.S. EPA, 1976). The reliability of these release estimates was assumed to be ± 30 percent (U.S. EPA, 1976). Prior to the enactment of legislation, approximately 132,000 metric tons of PCBs were buried in unsecure sanitary landfills (U.S. EPA, 1976). This total was comprised of 50,000 metric tons from capacitor and transformer production wastes, 36,000 metric tons from disposal of obsolete electrical equipment, and 46,000 metric tons from disposal of material from open-end applications. An additional 14,000 metric tons of PCBs, although still in service in various semi-closed and open-end applications in 1976 were estimated to ultimately be destined for disposal in landfills.

Table 1. Estimated U.S. Usage of PCBs by Use Category (1930-1975)

Category	Type of Product	Total Use
Completely closed electrical systems	Transformers, capacitors, electrical insulating and cooling applications	61% before 1971 100% after 1971
Semi-closed applications	Hydraulic fluids, heat transfer fluids, lubricants	13% before 1971 0% after 1971
Open-end applications	Plasticizers, surface coatings, ink and dye carriers, adhesives, pesticide extenders, carbonless copy paper, dyes	26% before 1971 0% after 1971

Source: NRC (2000)

Table 2. Percentage of Total Aroclor Production Contributed by Specific Aroclors during the Years 1957 - 1977

Aroclor	1957-1977 U.S. Production (%)
1016	12.88
1221	00.96
1232	00.24
1242	51.76
1248	06.76
1254	15.73
1260	10.61
1262	00.83
1268	00.33

Source: Brown (1994)

II.PCB Congener Composition of Aroclors

Frame et al. (1996) has reported on the detailed analyses of the PCB congener distributions present in Aroclors 1016, 1242, 1248, and 1254. Because of variation to the chlorination process during chemical synthesis, no two batches of the same Aroclor had identical PCB congener distributions. In fact, substantial differences in congener profiles between batches of the same Aroclor couldcan lead to significant differences in biological effects (Kodavanti et al., 2001). Nevertheless the work by Frame et al. (1996) has yielded typical congener patterns present in the PCB formulations. The typical percent distribution of congeners by PCB homologue groupings is depicted in Table 3. Note that the most abundant homologue groups are the di- and tri-chlorinated biphenyls for the low chlorinated Aroclors (1016 and 1242) while penta-chlorinated biphenyls were more abundant in the higher chlorinated Aroclors (1248, 1254 and 1260). Tetra-chlorinated biphenyls were abundant in both low chlorinated and higher chlorinated Aroclors.

Table 3. Typical PCB Homologue Composition (% wt) of Five PCB Aroclors

PCB Homologue	Aroclor 1016 (%)	Aroclor 1242 (%)	Aroclor 1248 (%)	Aroclor 1254 (%)	Aroclor 1260 (%)
Mono-CB	0.7	0.8	0	0	0
Di-CB	17.5	15.0	0.4	0.2	0.1
Tri-CB	54.7	44.9	22.0	1.3	0.2
Tetra-CB	26.6	32.6	56.6	16.4	0.5
Penta-CB	0.5	6.4	18.6	53.0	8.6
Hexa-CB	0	0.3	2.0	26.8	43.4
Hepta-CB	0	0	0.6	2.7	38.5
Octa-CB	0	0	0	0	8.3
Nona-CB	0	0	0	0	0.7
Deca-CB	0	0	0	0	0

Source: Frame et al., 1996

III.Alterations of PCB congener profiles as a result of environmental weathering

In the environment, PCBs occur as mixtures of congeners, but their composition will differ from the commercial Aroclors. The chemical and physical properties largely effects the environmental distribution of PCBs. The National Research Council (2000) recently reviewed the fate processes that tend to change the environmental mixtures of PCBs from what was initially released into the environment. The term, 'weathering', refers to the sum effect of these fate processes. When released into the environment, PCBs tend to partition to the organic component of soil, water and sediment. Within an aquatic system, PCBs can exist in three phases: freely dissolved in water; associated with dissolved organic carbon in the water column; and sorbed to particles (NRC, 2000). Freely dissolved light molecular weight PCB congeners may volatilize from the water and into the atmosphere. PCB congeners sorbed to organic carbon in the water column can cross the sediment-water interface and can move below the surficial sediments through the process of diffusion (NRC, 2000). Particle-bound PCB congeners eventually settle to become incorporated into the sediments. The NRC (2000) has noted the following generalizations with respect to the environmental distribution of PCB congeners:

1.The less chlorinated PCB congeners are more water soluble, more volatile and more susceptible to biodegradation. This tends to cause lower concentrations of these PCB congeners in sediments as compared with their distribution in the Aroclor that was discharged into the environment.

2.Higher chlorinated PCB congeners are less soluble, sorb more readily to organic substrates, are less volatile and less susceptible to biodegradation. These PCB congeners are persistent in sediments and tend to bioaccumulate into ecological food chains.

3.As a result of weathering, the PCB congener mixtures that occur in the environment differ substantially from the PCB congener composition of the original industrial release (Bazzanti et al., 1997).

IV.Alterations of PCB congener profiles as a result of bioaccumulation and biomagnification in ecological food chains

Measures of Aroclor mixtures or total PCB concentrations may not provide adequate data on PCB exposure and health risks to wildlife. Although there are 209 possible congeners, only about half are prevalent in the environment and, of those, only a limited number both accumulate in animal tissues and exhibit significant toxic effects (McFarland and Clarke, 1989; Chiu et al., 2000; Letcher et al., 2000). Furthermore, differences in uptake, metabolism and bioaccumulation of PCB congeners can lead to significant differences betweenin congener profiles in predators feeding high on aquatic food webs and profiles than in contaminated sediments in the same ecosystems or in the original Aroclor mixtures (NRC, 2000; Chiu et al., 2000).

Toxicity of different congener groups

Accurate information on specific congener body burdens is important as toxicological effects vary greatly. PCB congener-specific toxic effects in mammals are believed to include developmental and reproductive toxicity, dermal toxicity, endocrine effects, hepatotoxicity and carcinogenesis (Safe, 1993). Coplanar congeners, those having two para-, two or more meta- and no ortho- chlorine substituents, and their mono-ortho analogs may be responsible for much of the observed toxicity of PCB mixtures (Safe, 1994). Coplanar PCBs behave like dioxins such as TCDD by binding to the aryl hydrocarbon (Ah) receptor in the liver. Because of this shared mechanism, the toxic equivalency factor (TEF) approach has been used for regulatory purposes to estimate the environmental and human health risks of particular PCB congeners (Safe, 1994). Several different methods of calculating TEFs have been developed using particular animal species and toxic endpoints (Leonards et al., 1995). There are limitations to the predictive value of the TEF approach for PCB mixtures as the biological activity of some congeners may change in the presence of other congeners (Safe, 1994, 1998). In general, the three congeners considered most toxic, based on dioxin-like activity, are the non-ortho (coplanar) PCBs with the IUPAC numbers 77 (chlorinated on carbons 3,3',4,4'), 126 (3,3',4,4',5) and 169 (3,3',4,4',5,5') (McFarland and Clarke, 1989). Some congeners may cause toxic effects indirectly through a variety of mechanisms involving the cytochrome P450 (CYP) mixed-function oxidase system (Letcher et al., 2000). While induction of CYP may help to remove contaminants, it may also harm the organism by turning otherwise nontoxic contaminants into cytotoxic or genotoxic metabolites (McFarland and Clarke, 1989). In addition, ortho-substituted congeners may have neurotoxic effects (Kodavanti et al., 2001).

Persistence and bioaccumulation of different congeners

PCB mixtures change as these contaminants move through abiotic media into food chains (Chiu et al., 2000; NRC, 2000). Some congeners exhibit preferential uptake, metabolism or bioaccumulation by different organisms (Jackson et al., 1998, 2001; Traas et al., 2001; Willman et al., 1997). Organisms acquire PCBs either through contact with or ingestion of contaminated sediments, water or soil, or through their food. Once the PCBs enter an organism, individual congeners are either cleared through metabolism and/or excretion or are sequestered, usually in lipid tissues. The rate of clearance of a PCB congener through non-metabolic processes is usually inversely proportional to its preferential solubility in lipids, measured as the octanol-water partition coefficient K_{OW} (Thomann, 1989). Metabolic clearance also depends on chemical structure of the congener and the induction of appropriate enzyme pathways in the organism.

Several factors tend to influence the bioaccumulation tendency of different congeners, including the number of chlorine (Cl) substituents and their positions on the two phenyl rings. In general, the more chlorinated congeners exhibit a higher level of persistence in vertebrates and will concentrate to higher levels in tissues of predators than in the surrounding environmental media or prey organisms. This phenomenon has been observed in field populations of fish (salmon - Jackson et al., 2001), birds (cormorants - Guruge and Tanabe, 1997; seabirds - Braune et al., 2001) and mammals (seals - Bernt et al., 1999) and corroborated in controlled laboratory studies (rats - Kodavanti et al., 1998). The position of Cl substituents on the ortho, meta or para positions also affects bioaccumulation (Boon et al., 1994). Congeners can be classified as either persistent or readily cleared based on the absence or presence, respectively, of neighboring meta-para hydrogen substituents (m,p-H) on at least one phenyl ring (kestrels - Drouillard et al., 2001; weasel/otters - Leonards et al., 1998; cormorants - Guruge and Tanabe, 1997; crustaceans and fish - Porte and Albaiges, 1994). At the bottom of the food chain, phytoplankton were observed to preferentially take up coplanar congeners rather than those with ortho- chlorine substituents (Swackhamer and Skoglund, 1991). The effect of degree of chlorination at ortho positions on bioaccumulation is more complex and variable in vertebrates (Bruhn et al., 1995; Boon et al., 1994).

It should be stressed that patterns of persistence of certain congeners do not hold across species. For example, the highly toxic non-ortho PCBs congeners IUPAC 77, 126 and 169 are metabolized and not abundant in body tissues of some predators experiencing high levels of PCB exposure (seal - Nakata et al., 1997; salmon - Willman et al., 1997; porpoise - Bruhn et al., 1995) but congeners 126 and 169 do appear to preferentially bioaccumulate in other predator species (weasel/otters - Leonards et al., 1998; cormorants - Guruge and Tanabe, 1997). Some general patterns may, however, exist. In their review of the occurrence and abundance of PCB congeners across species, including humans, McFarland and Clarke (1989) observed that tetra-, penta- and hexa-clorinated congeners seemed to predominate in biological tissues. In addition, accumulated PCBs are further bioconcentrated at each succeeding trophic level in a food web, causing high- order predators to experience the highest overall environmental exposure to PCBs. The frequency and severity of adverse effects, however, depend not just on the level of exposure but also on the particular species' sensitivity to PCBs.

Biomagnification of different congeners in aquatic food chains

As PCBs are passed through a food chain, certain congeners are more likely to biomagnify than others (Jackson et al., 1998). How congener patterns change depends upon the number of trophic levels in a food web and the varying capacities of the different species to metabolize the contaminants. In an aquatic food web that included plankton, macro invertebrates, alewife and salmon in Lake Michigan, Jackson et al. (1998, 2001) found that the degree of biomagnification generally increased with the degree of congener chlorination. More specifically, the largest components of the total PCB mixture in plankton, the base of the pelagic food web, were tetra- and pentachlorobiphenyls, but in the macro invertebrates *Mysis* and *Diporeia* and in salmon, the PCB mixture was predominantly hexachlorobiphenyls. A similar pattern was observed in earlier research in Lake Michigan by Willman et al. (1997), in which penta-, hexa- and heptachloro congeners were more concentrated while trichloro congeners were depleted as the PCB mixtures moved from sediments to plankton to fish. Within groups of congeners with the same degree of chlorination (homologues), congeners with no or few ortho- chlorine substituents have shown a tendency to bioaccumulate in lower food webs in a study by Swackhamer and Skoglund (1991) but not in a study by Willman et al. (1997). In a Lake Ontario study focusing on mono- and non-ortho congeners, Metcalfe and Metcalfe (1997) found that these more toxic congeners were a larger percentage of the PCB profiles in plankton than in higher organisms in the food web. These congeners did preferentially bioaccumulate at certain trophic transfer points, specifically between invertebrates to fish and between fish and herring gulls.

V.Utility of PCB congener-specific analyses - an example

Reproductive toxicity of PCBs in mink

The limitations of wildlife risk assessments based only on total PCBs is illustrated in the case of mink (*Mustela vison*). Mink are fish-eating mammals and may be exposed through their diet to high levels of PCBs in contaminated ecosystems (Giesy et al., 1994). Mink are highly sensitive to PCBs and experience adverse reproductive effects including reduced litter size and high (up to 100%) kit mortality even when exposed to fairly low levels of PCB contamination in their diet (Heaton et al., 1995; Restum et al., 1998; Brunstrom et al., 2001). PCB concentrations in the food sources of wild populations of mink have been assessed in the Great Lakes region, while the practice of mink farming has allowed controlled laboratory experiments to determine the effects of PCBs on mink directly. Estimates of reproductive risks from PCB congeners can be based on analyses of diet or on mink body burdens. The reproductive effects appear to be caused by the dioxin-like congeners (Brunstrom et al., 2001). Ortho-congeners such as IUPAC 153 (2,2',4,4',5,5') and IUPAC 136 (2,2',3,3',6,6') may exhibit neurological effects (Aulerich et al., 1985).

In their review of recent literature, Giesy and Kannan (1998) observed that laboratory mink feeding studies using commercial Aroclor mixtures calculated higher low/no observable effect levels (LOEL/NOEL) and EC_{50} than did studies using weathered PCB mixtures as found in wild food sources (fish). In other words, weathered PCB mixtures were more toxic than the commercial mixtures, indicating that the congener profile changed as the contaminants moved through abiotic media and into the aquatic food web (e.g., Giesy et al., 1994). In an earlier review of experimental data, Leonards et al. (1995) found it difficult to determine a dose-response curve or reference dose for reproductive effects such as litter size or kit survival based on total PCB in the mink diet. However, a dose-response curve that matched laboratory observations could be calculated based on mink whole-body concentration of dioxin-like PCB congeners estimated using TEF calculations developed by Safe (1993). Further laboratory work by Brunstrom et al. (2001) confirmed that reproductive effects in mink are correlated with high levels of non- and mono-ortho-substituted-biphenyls (dioxin-like congeners) in their food, while no reproductive effects are observed among mink exposed to high concentrations of 2-4-ortho-substituted-biphenyls only. These studies clearly indicate the importance of using more refined measurements than total PCB concentrations to assess risks to sensitive wildlife.

VI.Conclusions

- PCB congener-specific data provide the best and most scientifically defensible basis for evaluating the ecological hazards that may be associated with PCB contamination in the environment. Information and examples presented in this memorandum gives scientific support to this premise.

- The weathering of PCBs, coupled with PCB bioaccumulation in ecosystems, considerably alters the mixture of PCBs congeners present in the environment. This means that, with the passage of time, the PCB congener patterns that initially comprised commercial PCB formulations are less likely to resemble the PCB congener patterns currently observed in the environment.

- Specifying the PCB congener profiles in environmental samples adds important information to the risk assessment process that otherwise would be obscured by only reporting Aroclor equivalents or total PCBs in the samples. PCBs exhibit a wide spectrum of toxicologic effects in various species, including humans (ATSDR, 2000). This has created two major groups of PCB congeners: 1) the dioxin-like (co-planar) PCBs, and (2) the non-dioxin-like PCBs. In specifying the PCB congener profiles for purposes of human health and ecological risk assessments, such groupings are useful.

- There is currently insufficient data upon which to generalize a pattern of occurrence of specific mixtures of PCB congeners present in all environmental media and in all biological tissues. Although this may change as PCB congener-specific analyses become more common in environmental studies, there is not yet an adequate scientific basis upon which to reconstruct likely congener patterns based on historical measurements that only report Aroclors and/or total PCBs present in the sample. It is recommended that additional research be directed towards addressing the question as to whether PCB congener patterns can be associated with specific environmental media or biological matrices. For example, can reference PCB congener profiles be developed in such a way that consistently represents the likely distribution of PCB congeners within a particular biological matrix such as adipose tissue, or a particular medium like soil, sediment, or air? If such patterns exist, then it may be possible to define a subset of specific PCB congeners that should be routinely identified and quantified in particular environmental matrices. A second aspect of this is to determine if a relationship exists between Aroclor standards or Total PCB measurements and the reference PCB congener mixtures of a particular matrix. This would increase the likelihood that PCB congener distributions could be reconstructed from historical measurements that have only reported data in terms of total PCBs or as commercial Aroclor equivalents. Until research has reached a point where one can readily identify clear and unambiguous PCB congener patterns in all environmental matrices, it is not possible to reach a firm conclusion as to the scientific validity of retrospectively reconstructing the likely PCB congener distributions in these historical environmental studies.

- Current state-of-the-art laboratory methods makes it possible to analytically identify and quantitate the presence or absence of all 209 PCB congeners in environmental samples (e.g., EPA Method 1668A). The overarching question then shifts away from analytical chemistry capabilities to one of defining a subset of 209 PCB congeners that should be routinely identified as PCB congener mixtures in specific environmental media and biota. This can only be addressed through further research directed at definitively identifying PCB congeners of concern from the perspective of persistence in the environment and toxicity to humans and wildlife.

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